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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 03/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No. 09/871,610	Applicant(s) MCGALL ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 December 2003 has been entered.

Status of the Claims

2. This action is in response to papers filed 22 December 2003 in which claims 1, 14 and 15 were amended. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 26 August 2003 are withdrawn in view of the amendments and new grounds for rejection. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 1-15 are under prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is vague and indefinite what is meant by the phrase "less than about 1 cm² (mm²)". The phrase "less than" typically indicates a maximum point. The phrase "less than" however, is contraverted by the term "about" which implies that values above and below 1 cm² (mm²) are permitted. Further, the extent of variance permitted by "about" is unclear in this context. In Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (CAFC 1991), the CAFC stated, "The district court held claims 4 and 6 of the patent invalid because their specific activity limitation of "at least about 160,000" was indefinite". After review, the CAFC states "We therefore affirm the district court's determination on this issue." Thus, the CAFC found the phrase "at least about" indefinite where the metes and bounds of the term were not defined in the specification. As such, the meets and bounds of the instantly claimed "less than about" is indefinite.

Claim Rejections - 35 USC § 102/103

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-7, 9-15 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Winkler et al (U.S. Patent No. 5,885,837, issued 23 March 1999).

Regarding Claim 1, Winkler et al disclose a method of preparing a nucleic acid array on a support (Column 1, line 64-66), the method comprising: activating a region of the support, attaching a nucleotide having a masked reactive site linked to a protecting group to a first region and repeating the activating and attaching on other regions of the support. The method further comprising removing the protecting group to provide an unmasked nucleotide, binding an additional nucleotide to the unmasked nucleotide and repeating the removing and binding on regions of the support to prepare a nucleic acid array (Column 9, line 12-Column 10, line 5) wherein the support is rotated about an axis perpendicular to the surface by an amount of from about 20 degrees to about 180 degrees, said rotating being prior to, coincident with or subsequent to either binding or attaching steps wherein the support has a different rotational position relative to a previous step (Column 9, lines 39-51). Winkler et al further teach the method wherein the support surface is maintained in a position which permits the reagent

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fluid to flow through channels during the attaching or binding steps (Column 11, lines 21-65) and the flow path is illustrated as being vertical (Fig. 6a/6b).

The preceding rejection is based on judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because Winkler et al is silent with regard to vertical position of the support surface. However, the vertical position recited in Claim 1 is deemed to be inherent in the flow through channels of Winkler et al because they specifically teach the flow channels lead “up to the synthesis chamber” (Column 11, lines 42-43) which clearly suggests that the flow channels (of the support) are vertically positioned.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to position the support comprising flow channels in a vertical position to thereby provide for reagent flow through the channels via gravitational force. Winkler et al teach some embodiment wherein the reagent is flowed through the channels via vacuum pumping (Column 8, lines 9-23). However, they teach that the pumping can create undesired “dead spots” in the flow channels (Column 10, lines 43-42). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to position the channels in a vertical position thereby allowing reagent flow via gravitational force and eliminating the “dead spots” created using vacuum pumping as desired by Winkler et al (Column, 10, lines 42-43).

The burden is on applicant to show that the claimed vertical position is either different or non-obvious over that of Winkler et al.

Regarding Claim 2, Winkler et al disclose the method wherein the support is rotated subsequent to at least 50% of the attaching or binding i.e. following monomer addition, the substrate is washed and rotated and the monomer addition steps are repeated (Column 9, lines 39-54).

Regarding Claim 3, Winkler et al disclose the method wherein the support is rotated subsequent to at least 80% of the attaching or binding i.e. following monomer addition, the

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substrate is washed and rotated and the monomer addition steps are repeated (Column 9, lines 39-54).

Regarding Claim 4, Winkler et al disclose the method wherein the support is rotated from about 75 to about 105 degrees i.e. 0 to 180 (Column 10, lines 40-45).

Regarding Claim 5, Winkler et al disclose the method wherein the support is rotated in an amount of about 90 degrees i.e. 0 to 180 (Column 10, lines 40-45 and Column 14, lines 9-10).

Regarding Claim 6, Winkler et al disclose the method wherein the support is vertical (see above discussion regarding Claim 1) and rotated in an amount of about 90 degrees i.e. 0 to 180 (Column 10, lines 40-45 and Column 14, lines 9-10).

Regarding Claim 7, Winkler et al disclose the method wherein the support is a "substantially" square planar silica chip (Column 5, lines 18-26; Column 7, lines 6-7; Column 8, lines 42-54) wherein the support is vertical (see above discussion regarding Claim 1) and rotated in an amount of about 90 degrees i.e. 0 to 180 (Column 10, lines 40-45 and Column 14, lines 9-10).

Regarding Claim 9, Winkler et al disclose the method wherein at least 10 different nucleic acids are synthesized on the surface (Column 10, lines 52-60).

Regarding Claim 10, Winkler et al disclose the method wherein at least 100 different nucleic acids are synthesized on the surface (Column 10, lines 52-60).

Regarding Claim 11, Winkler et al disclose the method wherein at least 1000 different nucleic acids are synthesized on the surface (Column 10, lines 52-60).

Regarding Claim 12, Winkler et al disclose the method wherein at least 10,000 different nucleic acids are synthesized on the surface (Column 10, lines 52-60).

Regarding Claim 13, Winkler et al disclose the method wherein at least 100,000 different nucleic acids are synthesized on the surface (Column 10, lines 52-60).

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Regarding Claim 14, Winkler et al disclose the method wherein each localized area is less than about 1 cm² (Column 5, lines 36-51).

Regarding Claim 15, Winkler et al disclose the method wherein each localized area is less than about 1 mm² (Column 5, lines 36-51).

8. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamble et al (U.S. Patent No. 5,981,733, issued 9 November 1999) in view of Winkler et al (5,677,195, issued 14 October 1997).

Regarding Claim 1, Gamble et al disclose a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support said synthesis comprising: activating a region of the support, attaching a nucleotide to a first region, said nucleotide having a masked reactive site linked to a protective group, repeating steps of activating and attaching on other regions of the support whereby each of said other regions has bound thereto another nucleotide comprising a masked reactive site wherein said another nucleotide may be the same or different from that used in the first step, removing the protecting group from one of the nucleotides bound to one of the regions of the support to provide a region bearing a nucleotide having an unmasked reactive site, binding an additional nucleotide to the nucleotide with an unmasked reactive site, and repeating the steps of removing and binding until a desired plurality of nucleic acids is synthesized, each occupying a separate known region wherein the surface of the substrate is maintained in a position which is vertical or about 30 degrees of vertical and wherein the substrate is rotated around an axis perpendicular to said surface by an amount of from about 20 degrees to about 180 degrees, said rotating being done prior to and subsequent to at least one of said attaching and binding

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steps (Column 12, line 18-Column 13, line 54 and Claims 9 & 10) whereby said rotated support has a different position relative to the support in the prior attaching step (i.e. moved along the X-Y axis, Column 12, lines 52-54) and wherein at least one of said attaching or binding steps occurs after the support is rotated i.e. during synthesis, the support is cyclically moved between the jetting system and the reaction chamber, Column 5, lines 66-67).

Gamble et al further teach the method wherein the support is held in a vertical position for reagent delivery (Column 4, lines 21-34) whereby the entire surface of the substrate is coated with the reagent and wherein the reagents include any reagents necessary for synthesis (Column 4, lines 40-46) whereby the substrate is in a vertical position during activation step (a) and clearly suggests that the substrate may be in a vertical position during attachment step (b). Furthermore, Gamble et al clearly provide motivation to position the substrate in vertical position during the attachment step when they teach that a vertical position provides complete coverage of the activated area and eliminates bubbles in the reagent solution (Column 4, lines 21-34). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to vertically position the substrate of Gamble et al during the attachment step to thereby insure complete coverage of the activated area and to eliminate problematic bubbles as they desire (Column 4, lines 21-34).

Gamble et al teach the method wherein the rotated support has a different position relative to the support in the prior attaching step (i.e. moved along the X-Y axis, Column 12, lines 52-54) but they do not teach the rotated position is different from the previous attachment/binding step. However, Winkler et al teach a similar method comprising activating a region of the support, attaching a nucleotide having a masked reactive site linked to a protecting group to a first region, removing the protecting group to provide an unmasked nucleotide, binding an additional nucleotide to the unmasked nucleotide and repeating the removing and binding on regions of the support to prepare a nucleic acid array (Column 15, line 10-Column 16, line 21) wherein the support is rotated about an axis perpendicular to the

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surface by an amount of from about 20 degrees to a bout 180 degrees, said rotating being prior to, coincident with or subsequent to either binding or attaching steps wherein the support has a different rotational position relative to a previous step (Column 15, lines 53-67) to thereby produce different flow patterns across the substrate. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the rotation of Gamble et al with the rotation providing a different rotational position relative to the previous attachment/binding step of Winkler et al for the expected benefit of producing different flow patterns across the substrate as desired by Winkler et al (Column 15, lines 53-67).

Regarding Claims 2 & 3, Gamble et al disclose the method wherein said rotating is conducted prior to or subsequent to at least 50% (Claim 2) and at least 80% (Claim 3) of said attaching and binding (Column 12, line 18-Column19, line 54 and Claim 9).

Regarding Claims 4 & 5, Gamble et al disclose the method wherein said rotating in an amount of from about 70 to about 105 degrees (Claim 4) and of about 90 degrees (Claim 5) (Column 12, line 18-Column19, line 54 and Fig. 12).

Regarding Claim 6, Gamble et al disclose the method wherein the interface is vertical (i.e. the support is vertical) and said rotating is an amount of about 90 degrees (Column 12, line 18-Column19, line 54; Claims 9 & 10; and Fig. 12).

Regarding Claim 7, Gamble et al teach the method wherein the substrate is square and a surface of the substrate (i.e. interface) is maintained in a position which is vertical or about 10 degrees of vertical (Column 12, line 18-Column19, line 54 and Claims 9 & 10) but they do not teach the substrate is substantially square silica chip. Winkler et al teach the similar method wherein the support is a "substantially" square planar silica chip (Column 14, lines 45-55) wherein the support rotated in an amount of about 90 degrees i.e. 0 to 180 (Column 15, lines 53-56 and Column 29, lines 3-5).

Regarding Claim 8, Gamble et al teach the method wherein the it is preferable that the substrate be positioned so that the maximal surface area of the substrate is covered by fluid

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rising from the bottom inlet port (Column 4, lines 21-34) but they do not teach the substrate held with one of the four vertices pointing downward. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the position of their substrate such that one of the vertices is pointing downward thereby maximizing the surface area covered by fluid rising across the surface for the obvious benefits of coving the entire surface of the substrate as they desire (Column 4, lines 30-34).

Regarding Claims 9-13, Gamble et al teach a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support (Column 12, line 18-Column 19, line 54 and Claims 9 & 10) and wherein each nucleic acid region have center-to-center spacing of 50 microns to 2 millimeters (Column 10, lines 12-15 and Column 12, lines 21-24) but they do not specifically teach the substrate comprises at least 10 different nucleic acids (Claim 9); at least 100 different nucleic acids (Claim 10); at least 1,000 different nucleic acids (Claim 11); at least 10,000 different nucleic acids (Claim 12); at least 100,000 different nucleic acids (Claim 13). However, high density arrays were well known in the art at the time the claimed invention was made as taught by Winkler et al teach their similar method wherein at least 100,000 different nucleic acids are synthesized on the surface (Column 17, lines 49-57). Winkler et al further teach the need exists for these high density arrays (Column 1, lines 12-20). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the high density array of Winkler et al to the array synthesis of Gamble et al based on the need for such arrays as taught by Winkler et al (Column 1, lines 12-20).

Regarding Claim 14, Gamble et al disclose the method wherein each different nucleic acid is in a region having an area of less than about 1 cm² (Column 10, lines 12-15 and Column 12, lines 21-24) and Winkler et al disclose the method wherein each localized area is less than about 1 cm² (Column 7, lines 10-24).

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Regarding Claim 15, Winkler et al disclose the method wherein each localized area is less than about 1 mm² (Column7, lines 10-24).

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741 until 13 January 2004. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-0507.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
February 25, 2004